



## King's Research Portal

DOI:

[10.1016/j.neubiorev.2017.04.004](https://doi.org/10.1016/j.neubiorev.2017.04.004)

*Document Version*

Peer reviewed version

[Link to publication record in King's Research Portal](#)

*Citation for published version (APA):*

Schuch, F. B., Deslandes, A. C., Stubbs, B., Gosmann, N. P., Silva, C. T. B. D., & Fleck, M. P. D. A. (2017). Factors that influence the neurobiological effects of exercise likely extend beyond age and intensity in people with major depression. *Neuroscience and Biobehavioral Reviews*.  
<https://doi.org/10.1016/j.neubiorev.2017.04.004>

### **Citing this paper**

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

### **General rights**

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

### **Take down policy**

If you believe that this document breaches copyright please contact [librarypure@kcl.ac.uk](mailto:librarypure@kcl.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.

## Accepted Manuscript

Title: Factors that influence the neurobiological effects of exercise likely extend beyond age and intensity in people with major depression

Authors: Felipe Barreto Schuch, Andrea Camaz Deslandes, Brendon Stubbs, Natan Pereira Gosmann, Cristiano Tschiedel Belem da Silva, Marcelo Pio de Almeida Fleck



PII: S0149-7634(16)30681-9  
DOI: <http://dx.doi.org/doi:10.1016/j.neubiorev.2017.04.004>  
Reference: NBR 2814

To appear in:

Received date: 1-11-2016  
Revised date: 23-3-2017  
Accepted date: 6-4-2017

Please cite this article as: Schuch, Felipe Barreto, Deslandes, Andrea Camaz, Stubbs, Brendon, Gosmann, Natan Pereira, Silva, Cristiano Tschiedel Belem da, Fleck, Marcelo Pio de Almeida, Factors that influence the neurobiological effects of exercise likely extend beyond age and intensity in people with major depression. *Neuroscience and Biobehavioral Reviews* <http://dx.doi.org/10.1016/j.neubiorev.2017.04.004>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

# Factors that influence the neurobiological effects of exercise likely extend beyond age and intensity in people with major depression

Felipe Barreto Schuch<sup>1,2,\*</sup>, Andrea Camaz Deslandes<sup>3</sup>, Brendon Stubbs<sup>4,5</sup>, Natan Pereira Gosmann<sup>2</sup>, Cristiano Tschiedel Belem da Silva<sup>2</sup>, Marcelo Pio de Almeida Fleck<sup>1,2</sup>

<sup>1</sup>Mestrado em Saúde e Desenvolvimento Humano, Unilasalle, Canoas, BR.

<sup>2</sup>Hospital de Clínicas de Porto Alegre, Porto Alegre, BR.

<sup>3</sup>Programa de Pós-graduação em Ciências do Exercício e do Esporte, Universidade Estadual do Rio de Janeiro, Rio de Janeiro, BR.

<sup>4</sup>Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, UK

<sup>5</sup>Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK

## Abstract

We recently conducted a comprehensive systematic review of neurobiological effects of exercise on major depressive disorder. A subsequent letter suggested that we should consider children and adolescent and raised the importance of how intensity may mediate neurobiological response in people with depression. Here, we discuss these comments regarding our review, in addition to proposing that other factors, such type, duration, frequency, and adherence, may also importantly influence neurobiological response, based on recent meta-analyses demonstrating these other aspects of physical activity also moderate dropout rates and effect sizes from exercise upon depression.

**Key words:** exercise, depression, neurobiological, adherence, intensity

## Commentary

We would like to thank Dr. Budde and colleagues for their interest in our recent systematic review investigating neurobiological effects of exercise on major depressive disorder (Schuch et al., 2016a). We agree with Dr. Budde and colleagues commentary (Budde et al.) that exercise has a positive impact on depression throughout lifespan including adolescents (Carter et al., 2016), working age adults (Schuch et al., 2016b) and older adults (Schuch FB et al., 2016). However, Dr. Budde and colleagues made two comments on our recent systematic review which we would like to briefly respond and then further expand upon.

First, Dr. Budde and colleagues state that we did not consider studies in children and adolescents regarding the neurobiological effects of exercise and depression. We would like to highlight to Budde et al that, regardless age, our review focused on neurobiological responses to exercise in people with depression. Whilst we fully agree that understanding the neurobiological effect of exercise in adolescence is essential, we have not found any paper that meets our eligibility criteria. Dr. Budde and colleagues have shown evidence of differences in biological mechanisms involved in depression in children and adolescents (e.g: hyperactivation of HPA axis) when compared to adults with depression. In addition, studies in healthy children have shown different neurobiological responses to exercise. In spite of those differences, the neurobiological effects of exercise in children and adolescents with depression were not investigated. We clarify that future studies on the neurobiological effects of exercise for depression in children are still required.

Second, Dr. Budde and colleagues highlight the importance of the intensity of exercise as an influencing factor on biological responses to exercise. We agree with this point as we outline in our original paper; however, as with any systematic review, we are only able to report on the available data meeting our study eligibility. In spite of that, other original studies have recently reported findings on this point, such as Meyers et al., (2016) who demonstrated that higher exercise intensity promotes a greater acute increase on Brain Derived Neurotrophic Factors (BDNF) than lower intensity exercise in people with depression. Also, previous studies have discussed that exercise intensity moderates the responses of several hormones (Kraemer and Ratamess, 2005), neurogenesis (Szuhany et al., 2015), inflammatory markers (Cullen et al., 2016; Eyre and Baune, 2012), and oxidative stress markers (Powers et al., 2016), as well as cortical activity (Ludyga et al., 2016) in healthy (non-depressed) humans or animal models. A recent extensive meta-analysis examining the antidepressant effect of exercise have indicated that moderate and higher intensity exercise can result in a greater antidepressant effect

(Schuch et al., 2016b); nevertheless, increasing intensity is known to threaten adherence and influence dropout rates (Stubbs et al., 2016). Thus, the success of any exercise intervention and the subsequent neurobiological response is dependent upon adherence, which is moderated by exercise intensity. Moreover, a recent meta-analysis of randomized controlled trials has shown that numerous other factors mediate the antidepressant effect of exercise, such as being aerobic only and interventions supervised by an exercise professional (e.g. physiotherapist, exercise physiologists) (Schuch et al., 2016b). In addition, these very same factors may also influence dropouts from exercise among people with depression (Stubbs et al., 2016). Thus, whilst intensity is important, some balance has to be struck when considering longevity and sustainability of exercise among people with depression and other important aspects also need to be considered.

In summary, we are thankful that Budde and colleagues took the time to review our article on exercise and neurobiological effects among people with depression. We agree that further research should address this important topic in children. We also concur that intensity can influence the neurobiological effects of exercise; notwithstanding, other factors, such as exercise type, duration, frequency, and adherence, may be equally important in acquiring an adequate antidepressant response from exercise.

## **Acknowledgement**

B.S. receive funding from the National Institute for Health Research Collaboration for Leadership in Applied Health Research & Care Funding scheme. M.F and A.D receive funding from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior.

## References

- Budde, H., Velasques, B., Ribeiro, P., Machado, S., Emeljanovas, A., Kamandulis, S., Skurvydas, A., Wegner, M., Does intensity or youth affect the neurobiological effect of exercise on major depressive disorder? *Neuroscience & Biobehavioral Reviews*.
- Carter, T., Morres, I.D., Meade, O., Callaghan, P., 2016. The Effect of Exercise on Depressive Symptoms in Adolescents: A Systematic Review and Meta-Analysis. *Journal of the American Academy of Child & Adolescent Psychiatry*.
- Cullen, T., Thomas, A.W., Webb, R., Hughes, M.G., 2016. Interleukin-6 and associated cytokine responses to an acute bout of high-intensity interval exercise: the effect of exercise intensity and volume. *Applied Physiology, Nutrition, and Metabolism* 41, 803-808.
- Eyre, H., Baune, B.T., 2012. Neuroimmunological effects of physical exercise in depression. *Brain, Behavior, and Immunity* 26, 251-266.
- Kraemer, W.J., Ratamess, N.A., 2005. Hormonal responses and adaptations to resistance exercise and training. *Sports Med* 35, 339-361.
- Ludyga, S., Gronwald, T., Hottenrott, K., 2016. Effects of high vs. low cadence training on cyclists' brain cortical activity during exercise. *Journal of Science and Medicine in Sport* 19, 342-347.
- Meyer, J.D., Ellingson, L.D., Koltyn, K.F., Stegner, A.J., Kim, J.S., Cook, D.B., 2016. Psychobiological Responses to Preferred- and Prescribed-Intensity Exercise in MDD. *Med Sci Sports Exerc*.
- Powers, S.K., Radak, Z., Ji, L.L., 2016. Exercise-induced oxidative stress: past, present and future. *The Journal of physiology*.
- Schuch FB, Vancampfort D, Rosenbaum S, Richards J, Ward PB, Veronese N, Solmi M, Cadore EL, B, S., 2016. Exercise for depression in older adults: a meta-analysis of randomized controlled trials adjusting for publication bias. *Rev Bras Psiquiatr* 0, 0.
- Schuch, F.B., Deslandes, A.C., Stubbs, B., Gosmann, N.P., Silva, C.T., Fleck, M.P., 2016a. Neurobiological effects of exercise on major depressive disorder: A systematic review. *Neuroscience & Biobehavioral Reviews* 61, 1-11.
- Schuch, F.B., Vancampfort, D., Richards, J., Rosenbaum, S., Ward, P.B., Stubbs, B., 2016b. Exercise as a treatment for depression: A meta-analysis adjusting for publication bias. *J Psychiatr Res* 77, 42-51.
- Stubbs, B., Vancampfort, D., Rosenbaum, S., Ward, P.B., Richards, J., Soundy, A., Veronese, N., Solmi, M., Schuch, F.B., 2016. Dropout from exercise randomized controlled trials among people with depression: A meta-analysis and meta regression. *Journal of Affective Disorders* 190, 457-466.
- Szuhany, K.L., Bugatti, M., Otto, M.W., 2015. A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *Journal of Psychiatric Research* 60, 56-64.